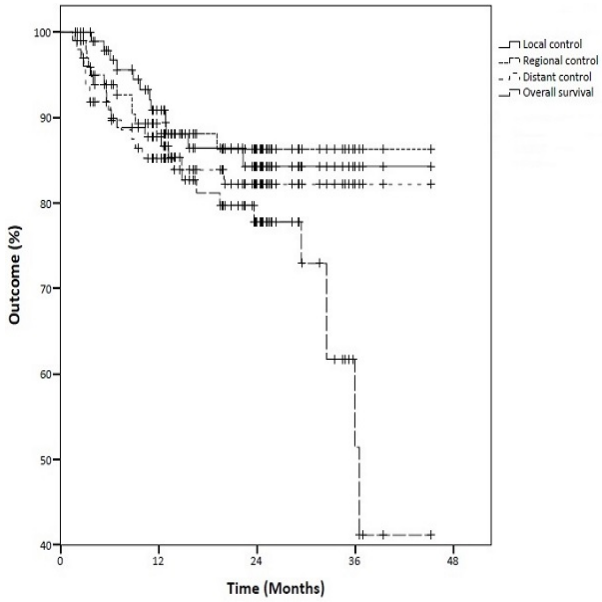
Purpose or Objective: A multicentre prospective randomized phase II trial investigated whether a 3-phase adaptive IMRT-scheme using reduced volumes of elective neck could reduce toxicity without compromising disease control compared to standard non-adaptive IMRT. We report on disease control and toxicity at 6 and 12 months of follow-up.

Material and Methods: All patients were primarily treated with IMRT ± chemotherapy for head and neck squamous cell carcinoma with a 2 Gy-equivalent dose of 40 Gy to the elective neck. The dose to the high-risk volume was not reduced. In the adaptive de-escalation (AD) arm, elective neck volumes were reduced based on a lower theoretical risk of subclinical disease and replanning was done after 2 and 4 weeks. In the control (C) arm, IMRT without adaptations and with standard volumes of elective neck was performed.
All statistics were performed using Fisher's exact test and Kaplan-Meier analysis (SPSS v. 23).

Results: Patiënts, tumor and treatment characteristics can be found in Table 1.
Before 1 year of follow-up, 12 patients deceased due to aspiration (n=1), tumor progression (n=8) or intercurrent disease (n=3).
At 6 months, we observed grade (G) ≥2 dysphagia in 3% and 6% (p = 1.0), G≥2 xerostomia in 40% and 34% (p = 0.81) and G≥2 fibrosis in 6% and 6% (p = 1.0) in the AD- and C-arm, respectively. At 12 months, we observed grade G ≥2 dysphagia in 17% and 3% (p = 0.09), G≥2 xerostomia in 43% and 28% (p = 0.28) and G≥2 fibrosis in 10% and 9% (p = 1.0) in the AD- and C-arm, respectively.
Local (LC), regional (RC) and distant control (DC) and overall survival (OS) for the whole group are given in Fig. 1. LC, RC, DC and OS were 86%, 84%, 82% and 74% in the AD-arm and 90%, 92%, 86% and 78% in the C-arm, respectively. All p-values were > 0.05. Regional relapse was observed in 8 (AD) and 4 (C) patients: 5/12 were isolated regional relapses (3 in the AD- and 2 in the C-arm) of which 3/5 isolated relapses were seen in the initial GTV of a pathological lymph node, 1/5 in the irradiated elective neck in the C-arm and 1/5 in the AD-arm in a region of the neck that would have been irradiated in the C-arm; salvage neck dissection was successfully performed. Seven regional relapses were combined with local recurrence (n=3) or metastases (n=4).

	AD-arm (n=50)	C-arm (n=50)	p-value
Age (range; in years)	63,0 (38-84)	62,4 (38-83)	
Male/female	39/11	42/8	0.61
Site: - Oropharynx - Hypopharynx - Larynx - Oral cavity	 24 13 10 3	 25 10 14 1	0.56
HPV-status oropharynx - Negative - Positive - Unknown	 5 4 15	 8 5 12	0.76
T-staging - T1 - T2 - T3 - T4a - T4b	 1 16 15 16 2	 3 12 20 12 3	0.55
N-staging - N0 - N1 - N2a - N2b - N2c - N3	 11 2 0 16 19 2	 11 6 1 16 15 1	0.58
Pre-IMRT neck dissection	5	5	1.00
Concomitant systemic therapy - Cisplatin-based - Cetuximab	30 29 1	29 27 2	1.00



Conclusion: With a minimal follow-up of 1 year, no significant differences in RC, LC or DC or OS were observed between adaptive IMRT with reduced volumes of elective neck versus standard IMRT with non-reduced volumes, although 1 patient had an isolated regional recurrence in the non-treated elective neck. Unfortunately, the volume reduction and adaptive strategy did not result in a better late toxicity profile. We hypothesize that due to the large portion of patients with locoregionally advanced disease the treated neck volumes could not be sufficiently reduced in the whole group to achieve the desired gain in toxicity. Future analysis will now be started to elucidate this problem.

OC-0453

Phase II trial of de-intensified chemoradiotherapy for HPV-associated oropharyngeal cancer

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Purpose or Objective: We performed a prospective multi-institutional phase II study of a substantial decrease in concurrent chemoradiotherapy (CRT) intensity as primary treatment for favorable risk, HPV-associated oropharyngeal squamous cell carcinoma (OPSCC).

Material and Methods: The major inclusion criteria were: 1) T0-T3, N0-N2c, M0, 2) HPV or p16 positive, and 3) minimal/remote smoking history. Treatment was limited to 60 Gy intensity modulated radiotherapy with concurrent weekly intravenous cisplatinum (30 mg/m2). The primary study endpoint was pathologic complete response rate (pCR) based on required biopsy of the primary site and dissection of pretreatment positive lymph node regions, regardless of radiographic response. Power computations were performed for the null hypothesis that the pCR rate is 87% and N=40, resulting in a type I error of 14.2%. Secondary endpoint measures included physician reported toxicity (CTCAE), patient reported symptoms (PRO-CTCAE), quality of life

(EORTC QLQ-C30 & H&N35), and penetration aspiration scale (PAS) scores for modified barium swallow studies.

Results: The study population is 43 patients. The pCR rate was 86% (37/43). All 6 non-pCR cases were limited to microscopic foci of residual cancer: 1 primary site, 5 nodal. All patients are alive with no evidence of disease (median follow-up 21.3 months, range 4-41 months). Thirty-eight patients had a follow-up of at least one year. The incidence of acute CTCAE Grade 3/4 toxicity and PRO-CTCAE severe/very severe symptoms were: mucositis 34%/45%, pain 5%/48%, nausea 18%/52%, vomiting 5%/34%, dysphagia 39%/55%, and xerostomia 2%/75%. Grade 3/4 hematological toxicities were 11%. Mean pre and 6 month post CRT EORTC QOL scores were: Global 80/71 (lower worse), Pain (mouth, jaw, throat) 19/21 (higher worse), Swallowing 11/16, Coughing 17/26, Dry Mouth 16/68, and Sticky Saliva 6/49. Six months post CRT mean PRO-CTCAE scores for swallowing and dry mouth were mild and moderate, respectively. No patients reported their swallowing or dry mouth symptoms to be severe or very severe. 39% of patients required a feeding tube (none permanent) for a median of 15 weeks (5 - 22 weeks). There were no significant differences in PAS scores for thin, pureed, and solid foods before and after CRT.

Conclusion: Pathological CR rate with decreased intensity of therapy with 60 Gy of IMRT and weekly low-dose cisplatinum is very high in favorable risk OPSCC with evidence of decreased toxicity compared to standard therapies. (ClinicalTrials.gov, NCT01530997)

OC-0454

Clinical outcome in nasopharyngeal carcinoma patients with post-radiation detectable plasma EBV DNA

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Purpose or Objective: To investigate the long-term clinical behavior of nasopharyngeal carcinoma (NPC) patients with persistently detectable plasma EBV (pEBV) DNA after curative radiotherapy (RT) with/without chemotherapy.

Material and Methods: We screened 931 newly diagnosed NPC patients who finished curative RT and found 125 patients (13.4%) with detectable pEBV DNA one week after finishing RT. The clinical characteristics, treatment modality, subsequent failure patterns and survivals were analyzed.

Results: The levels of post-RT pEBV DNA for the studied population were in a very lower copy number (median 21, interquartile range 8-206 copies/mL). After a minimal follow-up of 52 months, the subsequent relapse rate was 64.8% (81/125) with distant failure predominantly and the median time to progression is 20 months for all 125 patients. Thirty-two of 39 (82.1%) patients with post-RT pEBV DNA ³ 100 copies/ml developed tumor relapse later, whereas 57.0% (49/86) patients with post-RT pEBV DNA < 100 copies/ml had tumor relapse (*P*=0.0065). The 5-year rates of overall survival (OS) were 20.5% and 62.9% for the patients with post-RT viral load ³ and < 100 copies/mL (HR, 0.22; 95% CI, 0.12 to 0.38; *P*<0.0001). Patients who received adjuvant chemotherapy (AdjCT) with oral tegafur-uracil experienced significant reduction in distant failures (66.2% vs. 31.6%; *P*=0.0001) but similar locoregional recurrences (*P*=0.234). The 5-year OS rates were 69.4% for the patients who received AdjCT compared with 33.2% for those of without AdjCT (HR, 0.38; 95% CI, 0.24 to 0.61; *P*<0.0001).

Conclusion: NPC patients with persistently detectable pEBV DNA after finishing RT have a higher rate of treatment failure. Levels of the post-RT pEBV DNA and administration of AdjCT affect the final outcome. Future trial should consider post-RT pEBV DNA levels as a stratification factor and investigate the role of AdjCT for the target population.

Proffered Papers: Physics 11: Dose measurement and dose calculation II

OC-0455

Development of activity pencil beam algorithm using nuclear reaction for innovative proton therapy

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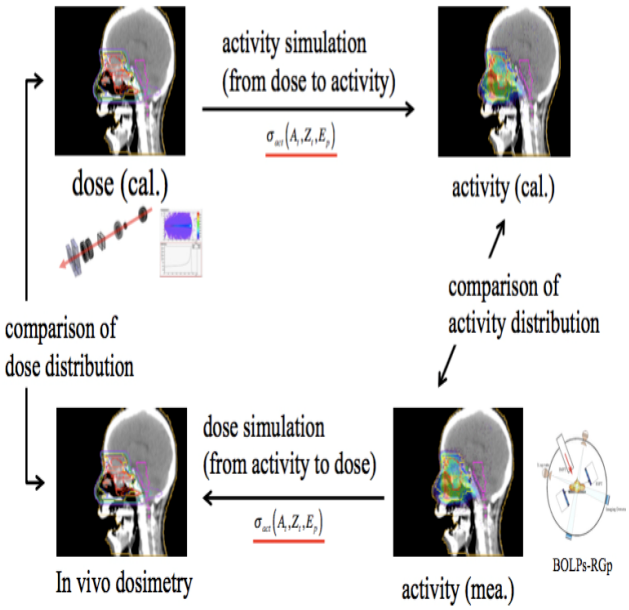
Purpose or Objective: Proton therapy is a form of radiotherapy that can be concentrated on a tumor using a scanned or modulated Bragg peak. To use this radiotherapy efficiently in a clinical context, it is necessary to evaluate the clinical proton-irradiated volume accurately. Therefore, a beam ON-LINE PET system (BOLPs) has been developed for activity imaging of various positron emitter nuclei generated from each target nucleus by target nuclear fragment reactions with irradiated proton beam. The purpose of this study is to develop an activity pencil beam (APB) algorithm for a simulation system for proton activated positron-emitting imaging in proton therapy.



Material and Methods: The APB algorithm was developed as a calculation algorithm of the activity distributions formed by positron emitter nuclei generated from target nuclear fragment reactions. Depth activity data of 12C nuclei, 16O nuclei, and 40Ca nuclei were measured with BOLPs after proton beam irradiation whose energies were 138, 179, and 223 MeV. Measurement time was about 5 h until the measured activity reached the background level.